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ON THE SPIROCHETAL INFECTION OF ULCERS IN CHINA *

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The occurrence in China of spirochete-infected ulcers of serious clinical importance was first observed by Assmy,¹ who in 1909 called attention to the presence of tropical ulcer in Chungking, a type of ulcer peculiar clinically and characterized by the presence of spirochetes and fusiform bacilli. Later, Logan² reported the frequent occurrence of the disease at Changteh.

The present work was begun to ascertain principally the geographical distribution of the disease. It is based on smears from unselected cases of ulcers of the extremities, contributed for the most part by members of the China Medical Missionary Association, to whom I wish to acknowledge my great indebtedness. I am indebted especially to Dr. H. S. Houghton, chairman of the committee of research. A word of explanation is necessary as to why the material was limited to ulcers of the extremities, in view of the fact that ulcers of the genitalia, of the same general character as tropical ulcer, are known to occur. However probable it may be, it has not been proved that the infection in these cases is similar to that in cases of true tropical ulcer, and it was desirable to keep the subject as free from complications as possible. Second, it was feared that by admitting genital ulcers into the field of investigation a large amount of negative material from venereal infections would be received, which would alter the statistics on relative frequency. In a few instances smears of this character were included among those examined. Their number, however, is too small to appreciably affect the statistical value of the data. The smears, which were sent in without fixation, were fixed in methyl alcohol and examined after staining over night with Giemsa.

Altho the work was primarily intended as a study of tropical ulcer, it was soon found that it would be necessary to broaden it into a study

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1. China Med. Jour., 1909, 23, p. 384; Arch. f. Schiff. u. Trop. Hyg., 1909, 13, p. 657.

2. China Med Jour, 1911, 25, p. 224

of the subject of spirochetal infections of ulcers in general in view of the interesting diversity observed in the organisms of that sort. In all, six principal types of spirochetes have been observed.

Type A.—This is a long, tenuous organism, which typically possesses from three to four complete, regular convolutions of considerable amplitude (Figs. 1 and 2). It is on an average about 13μ long, but varies considerably from this figure in both directions. As a rule it takes a bluish stain with Giemsa's solution. Occasional

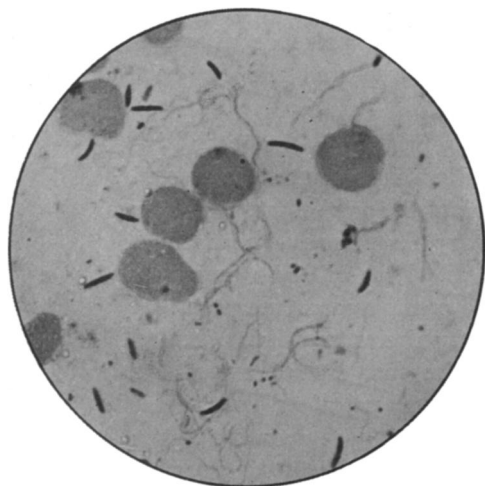


Fig. 1

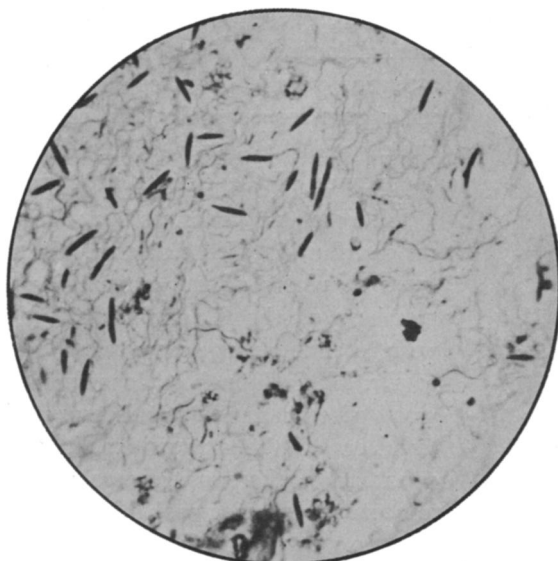


Fig. 2

Fig. 1.—Tropical ulcer, with spirochetes of Type A and fusiform bacilli of Type 1. Giemsa $\times 1000$.

Fig. 2.—Tropical ulcer, with spirochetes of Type A and fusiform bacilli of Type 1. Giemsa $\times 1000$.

smears are found with organisms of this sort stained violet, but this is probably due to irregularity in the stain. Individual organisms sometimes show variations in staining results, as some parts stain deeply while other parts stain scarcely at all. Again, the one organism is at times much thicker at one end than at the other. Scattered among the typical forms described are found spirochetes with perfectly regular convolutions, but much thicker and with tapering ends. These were believed by v. Prowachek,³ who studied the disease in

³ Arb. a. d. k. Gsndhtsamte, 1907, 26, p. 23.

Java, to represent sexual forms. What v. Prowachek considers as resting forms—spirochetes with terminal nodules—are also observed, altho the intermediate stages between these and the normal spirochetes, as described by v. Prowachek, and by Keysselitz and Mayer,⁴ have not been seen by the writer. Occasional organisms show a terminal flagellum. The bending of these spirochetes into irregular loops and volutes and their grouping together in tangled skeins are not infrequent.

There are several variants of this type. The first differs in that the convolutions are smaller, more numerous, and more irregular (Fig. 3). That this does not constitute a specific variation was shown

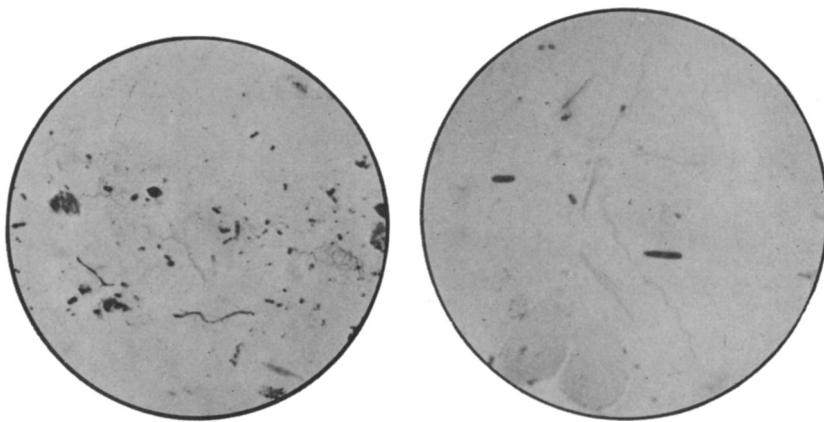


Fig. 3

Fig. 4

Fig. 3.—Irregularly convoluted spirochetes of Type A, with spirochetes of Type F near left margin. Giemsa $\times 1000$.

Fig. 4.—“Straight” organisms of Type A and associated bacilli of Types 1 and 3. Giemsa $\times 1000$.

by an organism of this type which was found linked end to end with one of the regularly convoluted type. The second variant is practically straight, as if a convoluted form had been subjected to tension (Fig. 4). This form occurs as a rule in large numbers in the specimens in which it is present at all. There is little reason to consider this as a separate type as it is found only in association with the convoluted forms and has every appearance of having been derived from them. Another variant, which quite possibly represents a different organism, has been seen only in specimens from Swatow, Kuangtung. It is characterized by great length (17μ average) and by more

4. Arch. f. Schiff u. Trop. Hyg., 1909, 13, p. 137.

numerous convolutions of great regularity and relatively slight amplitude (Fig. 5).

Since the organisms described by v. Prowachek and termed by him *Sp. schaudinni* are commonly regarded as the type of the spirochetes of tropical ulcer, it was of interest to compare the organisms observed in China with these, the more so as the drawings accompanying v. Prowachek's article show an organism considerably less tenuous

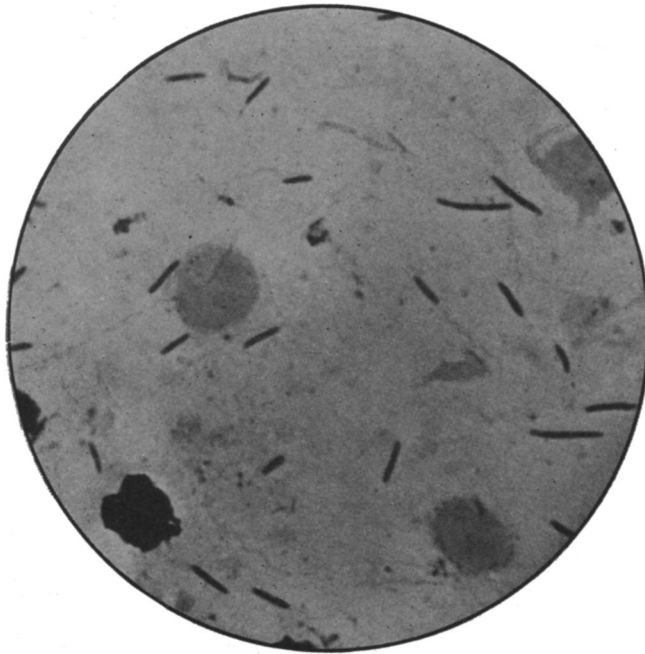


Fig. 5.—Spirochetes of Swatow type and fusiform bacilli of Type 1. Giemsa $\times 1000$.

than the Chinese form. This comparison was made possible by material kindly sent from Java by Dr. H. M. Neeb. The spirochetes in the Javanese specimens apparently differed in no respect from those of the Chinese specimens. The latter also appear to be similar to those described by Keysselitz and Mayer⁴ and Wolbach and Todd.⁵ They differ from the latter, however, as do the Javanese spirochetes, in having the nodular enlargement of the "resting forms"

5. Jour. Med. Research, 1912, 27, p. 27.

at or near the end of the spirochete, while in the forms from Zambesia described by the latter observers the nodules were more nearly central.

Type B.—This organism is a trifle longer and much thicker than Type A. It is irregularly convoluted and stains red or reddish violet with Giemsa. Its ends taper abruptly (Fig. 6).

Type C.—Like Type B, this spirochete stains red or reddish violet. It is a little thicker than Type A and is much shorter, seldom over $7\ \mu$ long. Further, it is characterized almost invariably by perfect regularity of convolutions, which are of small amplitude.

Type D.—This organism, met in only a few cases, is characterized by extreme tenuousness and the possession of only one or one and

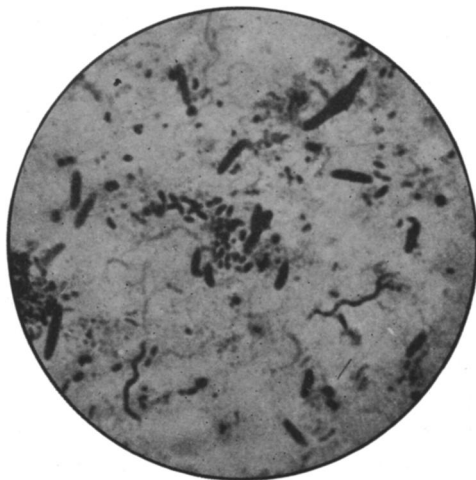


Fig. 6.—Spirochetes of Type A and B (latter in lower half of field) and fusiform bacillus showing central swelling. Giemsa $\times 1000$.

one-half complete convolutions of perfect regularity and great amplitude. It stains bluish violet.

Type E.—Organisms of this type have been met only twice. They are about as long as Type C, very thick, regularly and finely convoluted, with abruptly tapering ends, and they stain an intense blue.

Type F.—This organism is generally of the same tenuousness as Type A, but differs from it in that the former is as a rule irregularly and finely convoluted. It is of about the same length as Type C (Fig. 3). Organisms of this type differ considerably among themselves, and it is quite possible that it includes more than one type.

It is inadvisable, however, to risk undue multiplication of varieties on minor distinctions.

With all spirochetes that occur in large numbers, it is not unusual to find paired forms, to which reference has already been made, linked together end to end by a fine filament. These are the only unquestionable evidences of division that have been observed. Much more doubtful in this connection are the spirochetes with apparently forked ends, which are not infrequent.

Altho there are apparent exceptions, there occur along with the spirochetes certain distinctive bacilli. Following is a description of three of these bacilli:

1. Fusiform bacilli, which stain violet. These may be grouped into two subtypes, altho it is not always possible to differentiate sharply between them: (a) Cytoplasm uniform or finely granular. Sometimes slightly curved; at times forming chains of considerable length. Dimensions of single organism from $6-12\mu$ long, by 1μ in diameter. At times, particularly when forming chains, their ends becoming club-shaped, and they lose their fusiform appearance. Occasionally, they possess a pale-staining, median, transverse zone (Figs. 1, 2 and 5); (b) cytoplasm containing reddish metachromatic granules, usually two in number symmetrically arranged. These bacilli are also frequently curved. They are $3-8\mu$ long and a little less than 1μ in diameter.

2. Fusiform bacilli, much smaller than those of Type 1, with clear, blue-staining cytoplasm and reddish, sharply defined, metachromatic granules (organisms of the Plaut-Vincent type). These, too, differentiate into two fairly distinct subtypes: (a) Very small, very slender, usually with two metachromatic granules symmetrically arranged. Seldom over 4μ in length by 0.5μ , or less, in diameter; (b) longer than the foregoing, usually with more numerous metachromatic granules which frequently, tho not necessarily, are arranged in symmetrical pairs. From $6-9\mu$ long by about 0.5μ in diameter. Also, there are found filaments, sometimes very long, similar to (a) and (b). Usually, these are of greater diameter than the bacilli. While at times they form spirochete-like strands, their differentiation from those organisms never offers real difficulty.

3. Short, plump, violet-staining organisms, with rounded or cvoid ends (Fig. 4). Occasionally these seem to possess a terminal flagel-

lum. Both these and bacilli of Type 1 sometimes show a large, spherical, central swelling (Fig. 6).

This paper is based on the examination of 2,874 specimens, and of these 270, or 9.3 percent, have shown the presence of spirochetes of one or more types. Of these, Type A is the most frequent, occur-



Figure 7



Figure 8



Figure 9



Figure 10

Figs. 7-10.—Lesions of tropical ulcer.

ring in 237 specimens. Type B was found in 36, Type C, D, and E occur infrequently, in 11, 3, and 2 cases, respectively, and Type F is second in frequency only to Type A, which is found in 121 cases.

It must be noted that in only 121 specimens were two or more types of spirochetes found in the same specimen. Not much stress

can be laid on this, for, altho the specimens were examined carefully, usually several times, infrequently one spirochete of a certain type would be found in from 200-400 fields, and when the search is complicated by the presence of overwhelming numbers of one type, as sometimes occurs, associated organisms may easily be overlooked.

As to the numbers in which the spirochetes occur, the greatest variation is shown by Type A, which in some specimens occurs only once in several hundred fields and in others is so numerous as to form a felted mass, with all intermediate stages of frequency. Type B also shows much variation in frequency but is never as abundant as Type A. In some specimens Types C, D, and E occur only in comparatively small numbers. Type F, usually infrequent, is present at times in fairly large numbers, but never presents the striking pictures that Types A and B sometimes show.

Nothing definite could be established concerning the relationship between the fusiform bacilli and the spirochetes. The different types vary in frequency in different specimens, apparently without rule. Occasionally one or more will be absent from a given specimen, and in two smears, both from Hankow, the writer could discover no fusiform bacilli whatever, altho spirochetes of Type A were present in fairly large numbers. On the other hand, fusiform bacilli of all types, and especially of Type 2, have been found, sometimes in great abundance, in a number of specimens in which careful search failed to show the presence of spirochetes. The relationship between the fusiform bacilli and spirochetes is one of symbiosis, probably non-obligative on the part of the fusiform bacilli, possibly mutually so.

At the outset of this work it was decided not to request clinical data in the fear that the amount of extra work involved would result merely in the curtailment of the material received. For this reason little can be said of the clinical significance of the different types of spirochetes, and we assume, as seems probable, that the various morphological types represent different species. Enough data were obtained however, to show that typical tropical ulcer is usually at least associated with large numbers of organisms of Type A. Clinically, these ulcers, as met in China, possess the following principal features (Figs. 7-10): smoothly, steeply margined; edges somewhat infiltrated; the ground covered with grayish, foul-smelling sloughs, which when detached leave readily bleeding granulation tissue. Great pain is an almost constant feature. Logan divides them into two

classes: An acutely fulminating type, running a very rapid course, destroying all tissue down to the bone, and eventually involving the bone itself, and a more chronic type, slowly destroying the soft and bony tissues of the extremity.

In addition, cases are seen in which the infection remains superficial. In the writer's experience these cases, as the preceding, are usually characterized by much pain. The great majority of these infections are single, but multiple ones (auto-inoculation?) sometimes occur. In general, it may be said that the clinical picture of tropical ulcer as met in China is in conformity with that of other regions.⁶

The fact must be emphasized that conditions practically indistinguishable from the clinical standpoint, but without the peculiar



Fig. 11.—Phagedenic ulcer, not associated with spirochetal infection.

bacteriological findings, may occur. Material received from Changteh illustrates this (Fig. 11). It was accompanied by a history typical of the acutely fulminating type of tropical ulcer in every respect except the presence of pain. Smears from this case, however, showed no spirochetes, but a peculiar "bean-pod shaped" organism in almost pure culture. The identification of tropical ulcer from the microscopical viewpoint also offers difficulties. In the course of this work, sufficient data were obtained to make it almost certain that ulcers in which organisms of Type A occurred in small numbers were not as a rule to be regarded as tropical ulcer. As these organisms occur in

6. Some idea of the clinical features as well as the distribution of tropical ulcer may be gathered from the following references:

Regnault (Annam): *Arch. gén. de méd.*, 1904, 2, p. 2268.
 Fontoymont and Gourdran (Madagascar): *Presse méd.*, 1905, 13, p. 35.
 V. Prowachek (Java): *Arb. a. d. k. Gsndhtsamte*, 1907, 26, p. 23.
 Brault (Algiers): *Arch. f. Schiffs- u. Trop.-Hyg.*, 1907, 11, p. 612.
 Keysseltz and Mayer (German East Africa): *Ibid.*, 1909, 13, p. 137.
 Leboeuf (French Congo): *Bull. Soc. de Path. Exot.*, 1908, 1, p. 339.
 Lenz (German East Africa): *München. med. Wchnschr.*, 1908, 60, p. 2045.
 Stevenel (Zinder): *Bull. Soc. de Path. Exot.*, 1911, 4, p. 180.
 Carr (Persia): *Trans. Soc. Trop. Med.*, 1911-12, 5, p. 206.
 Bruce (Zambesia): *Jour. Trop. Med.*, 1911, 14, p. 1.
 Woldbach and Todd (Zambesia): *Jour. Med. Research*, 1912, 27, p. 27.

all intermediate stages of frequency, from once in several hundred fields to sufficient numbers to form felted masses, it is evident that to establish a certain criterion is difficult. The classification adopted in Table 1 was based on the presence in the smear of considerable numbers of spirochetes of Type A in predominating proportion. This appears to correspond in general to the clinical classification. A great deal of the difficulty is probably due to the necessity of identifying these spirochetes by morphology alone. The writer has found in one of a number of chancroid cases and in one of gonorrhoeal urethritis spirochetes indistinguishable from Type A (Figs. 12 and 13) present

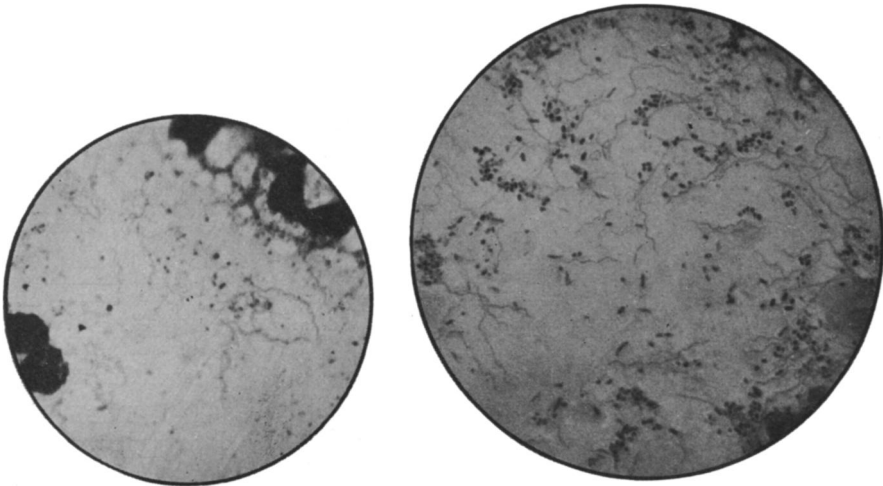


Fig. 12

Fig. 13

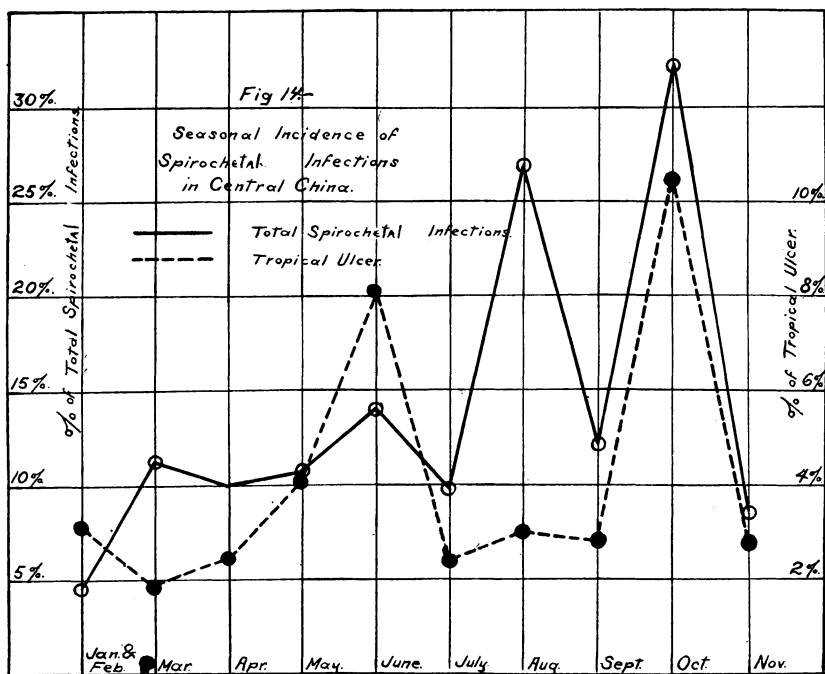
Fig. 12.—Spirochetes occurring in a case of chancroidal infection. Giemsa $\times 1000$.

Fig. 13.—Spirochetes associated with gonorrhoeal urethritis. Methylene blue $\times 1000$.

in considerable numbers, but without apparent influence on the clinical course of these lesions. In both of these specimens there was an absence of fusiform bacilli.

Of the remaining types of spirochetes, Type B was found as a predominating organism in enough cases to possibly warrant the suspicion that it has pathogenic properties. While Type F occurs at times in large numbers, as a rule it is associated with a plentiful and diverse flora and its pathogenicity is less probable. The remaining types of spirochetes occur in too small numbers to make probable any conclusions as to pathogenicity.

In regard to the geographical distribution of these infections, the northern third of China appears to be almost free from them. Out of 282 cases, six showed spirochetes. Of these, five came from barely north of the zone dividing China into three belts of equal latitude, and the sixth case from Peking seems so exceptional as to perhaps warrant the assumption that it was imported. None of these northern cases was of the microscopic type distinctive of tropical ulcer. Central China, using this term to mean the central eight of China's



twenty-four degrees of latitude, shows these infections in the greatest abundance and 221 cases, or 11.3 percent, of a total of 1,950, gave positive results. Seventy-six specimens, or 3.8 percent, could probably be diagnosed as tropical ulcer. All of the 39 centers, from almost all of which a representative lot of material was obtained, showed spirochetal infections. In some, such infections were much more frequent than in others. For instance, Changteh, which leads in frequency, showed 30 cases of spirochetal infection of a total of 66, with included 14 undoubted cases of tropical ulcer. The southern

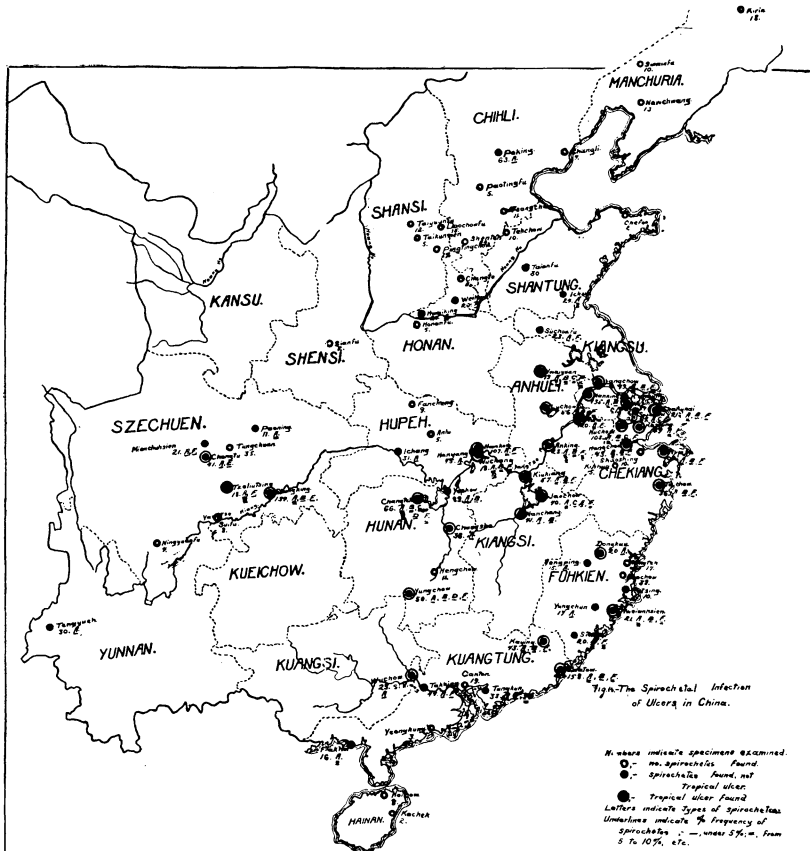
TABLE 1
GEOGRAPHICAL DISTRIBUTION OF SPIROCHETE-INFECTED ULCERS

Source	Total Specimens	Number Containing Spirochetes	Type A	Tropical Ulcer	Type B	Type C	Type D	Type E	Type F
Kirin.....	18
Sinminfu.....	10
Newchwang.....	13
Total from Manchuria	41								
Peking.....	63	1	1	1	1
Paotingfu.....	5
Changli.....	7
Tsangchow.....	11
Shenteh.....	24
Total from Chihli.....	110	1	1	1	1
Taiyuanfu.....	12
Liaochowfu.....	5
Taikuhsien.....	5
Pingling.....	17
Total from Shansi.....	39								
Tehchow.....	10
Taianfu.....	30
Chofoo.....	2
Ichowfu.....	24	4	4
Total from Shantung..	66	4	4						
Changte.....	5
Weihwei.....	20	1	1
Hwaiking.....	20	2	2
Honanfu.....	5
Total from Honan.....	50	3	3						
Sianfu.....	2
Total from Shensi.....	2								
Paoning.....	11	1	1
Mienchuhshien.....	21	1	1	1
Tungchwan.....	35
Chengtun.....	41	2	2	1	1	..
Szeliutsing.....	18	5	5	1	1
Chungking.....	134	21	19	5	1	7
Suifu.....	8
Ningyuanfu.....	4
Total from Szechuen...	272	30	28	7	1	1	9
Fancheng.....	9
Anlu.....	5
Ichang.....	31	1	1
Hankow.....	107	8	8	4	1
Wuchang.....	18	6	6	4	2	3
Total from Hupeh.....	245	17	15	8	2	4
Hwaiyuan.....	19	5	4	1	3	2	5
Luchowfu.....	56	13	13	1	2	..	1	..	9
Wuhu.....	120	10	9	3	4
Anking.....	23	8	7	4	2	5
Total from Anhwei.....	218	36	33	9	7	2	1	..	23

TABLE 1.—(Continued)

Source	Total Specimens	Number Containing Spirochetes	Type A	Tropical Ulcer	Type B	Type C	Type D	Type E	Type F
Hsuehowfu.....	23	2	2	1
Yangchow.....	49	10	5	2	2	8
Nanking.....	135	12	11	7	2	1	6
Kiangyin.....	17	2	2	1
Wusih.....	39	5	5	1	4
Soochow.....	67	3	1	2	2
Shanghai.....	218	19	16	7	2	8
Total from Kiangsu....	548	53	42	17	6	3	30
Kashing.....	49	4	4	3	3
Huchow.....	103	17	15	3	3	3	7
Hangchow.....	43	8	8	6	1	2
Shaoshing.....	10
Ningpo.....	103	3	3	1	3	3
Taichow.....	36	4	3	2	1	1
Kinhwa.....	5
Total from Chekiang..	349	36	33	15	8	3	16
Dongkau.....	20	1	1	1
Ningteh.....	17
Yengping.....	15	1	1
Foochow.....	38
Futsing.....	10
Yungchun.....	17	1	1
Hweianhsien.....	21	3	3	1	1	2
Sio khe.....	20	5	3	3
Total from Fukien.....	158	11	9	2	1	5
Kiukiang.....	57	5	4	1	1	1
Jaochow.....	40	7	6	3	..	1	..	1	3
Nanchang.....	41	2	2	2	1
Total from Kiangsi....	138	14	12	6	2	1	..	1	4
Yochow.....	89	3	2	..	1
Changteh.....	66	30	28	14	4	1	1	..	11
Changsha.....	36	1	1	1
Hengchow.....	11
Yungchow.....	50	5	2	2	1	..	1	..	1
Total from Hunan.....	252	39	33	17	6	1	2	..	12
Tengyueh.....	30	1	1	1
Total from Yunnan....	30	1	1	1
Kaying.....	43	3	3	1	1	2
Swatow.....	158	16	14	2	1	10
Canton.....	19
Takking.....	44	1	1	1
Tungkun.....	33	2	2	..	1	2
Yeongkong.....	3
Pakhoi.....	16	2	2
Hoihow.....	8
Kachek.....	2
Total from Kuangtung	326	24	22	3	3	15
Wuchow.....	25	1	1	1
Total from Kuangsi....	25	1	1	1
Unknown.....	5

zone of eight degrees of latitude has contributed 636 specimens from 22 centers, with 43, or 6.8 percent, showing the presence of spirochetes, and 9 specimens, or 1.4 percent, that can with some degree of probability be diagnosed as tropical ulcer. A number of cases of southern infections were contracted during sojourns in Singapore, as there was a large emigration of coolies thither from southeastern



China. A comparison of the incidence of spirochetal infections in central and southern China, as shown by the foregoing data, shows that these infections appear to be relatively more frequent in the former region. The same holds true for tropical ulcer in an even greater degree. Direct comparisons of absolute frequency cannot

be made with the present data, but the statement was made by several contributors from southern China that ulcerative lesions, in general, were rather uncommon there, and the much smaller amount of material sent from the south bears this out. Central China appears to be a richer field than southern China for spirochetal infections, and especially for tropical ulcer.

It is not possible to draw accurate deductions as to the seasonal prevalence of these infections from the material on which this article is based, as very little of it was dated. Approximate conclusions may however be drawn by arranging it according to time of receipt, allowing for the time of transportation from the more remote centers. The results obtained in this way for central China are presented in

TABLE 2
SEASONAL INCIDENCE OF SPIROCHETAL INFECTIONS OF ULCERS IN CENTRAL CHINA

Received	January and February	March	April	May	June	July	August	September	October	November
Total specimens	124	206	290	250	185	165	181	216	171	212
Total specimens containing spirochetes.....	6	23	39	27	26	16	35	26	55	18
Percentage.....	4.8	11.2	10.0	10.8	14.0	9.6	26.7	12.0	32.1	8.5
Type A.....	6	9	26	23	23	15	32	20	55	16
Percentage.....	4.8	4.3	9.0	10.2	12.4	9.1	24.4	10.7	32.1	7.5
Tropical ulcer...	4	4	7	10	15	4	4	6	18	5
Percentage.....	3.2	1.9	2.4	4.0	8.1	2.4	3.0	2.8	10.5	2.8
All other spiro- chetes.....	1	18	28	16	18	6	19	16	44	8
Percentage.....	0.8	8.7	9.6	6.4	9.7	3.6	14.5	7.4	25.8	4.4

Table 2, and graphically in Figure 15. Table 2 shows an increase in the number of spirochetal infections during the hot summer months. With tropical ulcer, on the other hand, the frequency appears to be fairly constant except in the case of material received during the months of June and October, when there is a decided increase. While it is impossible to assert that this is not accidental, the increase may be explained by the fact that rice planting in central China is in May and the harvest in August. This coincides in some measure with this apparent increase in frequency of tropical ulcer, after due allowance has been made for delays between collection of the specimens and arrival for examination. This result of greater incidence

in early and late summer is not in exact accordance with the opinion of a number of observers who are most familiar with the disease, who state that it is greatest during the hot season. Assmu and Kyritz⁷ state that the acutely phagedenic form is particularly frequent during the summer months, and as this is the most recognizable form, it may be the basis for this opinion.

SUMMARY AND CONCLUSIONS

Some six different morphological types of spirochetes have been found in ulcers of the extremities in China. Of these, one is known to be associated with a disease of fairly distinct clinical features. The pathogenic significance of the others is doubtful.

No constant relationship could be shown between the spirochetes and fusiform bacilli, and apparently either may occur independently of the other.

Spirochetes of the morphological type of those associated with tropical ulcer have been found in all degrees of abundance in smears from ulcers. When they are present in small numbers, the lesion apparently presents no distinctive features clinically.

In regard to geographical distribution, the north seems to be almost free from spirochetal infections. They appear to be particularly frequent in central China, and less frequent, tho present, in southern China. The distribution of tropical ulcer is similar.

Some evidence of increased frequency of spirochetal infections was observed during the summer months. Tropical ulcer appears to be most frequent in the early and late summer, tho the data on this point were not sufficiently accurate to warrant indisputable conclusions.

7. Arch. f. Schiffs- u. Trop.-Hyg., 1913, 17, p. 217.